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Application No. 09/423,037
Amendment dated December 10, 2008
Reply to Office Action of October 16, 2008

Docket No.: ASZD-P01-228

AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A method for identifying an inhibitor compound capable of reducing the interaction between a first component and a second component, comprising:
 - a) placing in contact:
 - i) a potential inhibitor compound;
 - ii) a first component which is an 8-10 amino acid fragment of a nuclear protein, wherein the fragment comprises only one signature motif B¹XXLL, in which B¹ is any natural hydrophobic amino acid, L is leucine, and X independently represents any natural amino acid, and the signature motif is a structural element of a nuclear protein that binds to a liganded nuclear receptor in the process of activating or repressing target genes, and the nuclear protein is a bridging factor responsible for an interaction between a liganded nuclear receptor transcription factor and a transcription initiation complex involved in regulation of gene expression provided that the fragment does not comprise a "NR-box" sequence XLXXLLXXXX.
 - iii) a second component which comprises a liganded nuclear receptor transcription factor or a fragment thereof, wherein the fragment comprises that part of the nuclear receptor which is capable of interacting with the nuclear protein through binding to the signature motif; and
 - b) detecting the presence or absence of inhibition of the interaction between ii) and iii).
2. (Cancelled)
3. (Previously Presented) A method according to claim 1, wherein B¹ is leucine or valine.
4. (Previously Presented) A method according to claim 3, wherein B¹ is leucine.
5. (Withdrawn) A method according to claim 1 wherein the signature motif is B²B¹XXLL wherein B² is a hydrophobic amino acid.

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6. (Withdrawn) A method according to claim 5, wherein B² is selected from isoleucine, leucine, methionine, phenylalanine, tryptophan, tyrosine and valine.
7. (Previously Presented) A method according to claims 1, 3, or 4, wherein the nuclear protein is a coactivator.
8. (Previously Presented) A method according to claim 7, wherein the coactivator is selected from RIP 140, SRC-1, TIF2, CBP, p300, TIF1, Trip1, Trip2, Trip3, Trip4, Trip5, Trip8, Trip9, p/CIP, ARA70 & Trip230.
9. (Previously Presented) A method according to claims 1, 3, or 4, wherein the transcription factor is a steroid hormone receptor.
10. (Previously Presented) A method according to claim 9, wherein the steroid hormone receptor is selected from oestrogen receptor, progesterone receptor, androgen receptor and glucocorticoid receptor.
11. (Previously Presented) A method according to claim 10, wherein the steroid hormone receptor is oestrogen receptor.
12. (Previously Presented) A method according to claims 1, 3, or 4, wherein the method is a 2-hybrid assay.
13. (Previously Presented) A method according to claims 1, 3, or 4, wherein the potential inhibitor compound is a member of a peptide library based on the signature motif.
14. (Withdrawn) A novel inhibitor identified according to the method defined in claim 1 which reduces the interaction between
 - a) a first region which is a signature motif on a nuclear protein, and

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b) a second region which is that part of a nuclear receptor which is capable of interacting with the nuclear protein through binding to the signature motif, wherein:

the nuclear protein is a bridging factor that is responsible for the interaction between a liganded nuclear receptor and the transcription initiation complex involved in regulation of gene expression;

the nuclear receptor is a transcription factor;

the signature motif is a short sequence of amino acid residues which is the key structural element of a nuclear protein which binds to the liganded nuclear receptor as part of the process of activation or repression of target genes.

15. (Withdrawn) An inhibitor according to claim 14 which is a peptide of less than 15 amino acid residues.

16. (Withdrawn) An inhibitor according to claim 15 selected from the group consisting of PQAQKSLQLLT (SEQ ID NO: 2), KLVQLTTT (SEQ ID NO: 3), ILHRLLE (SEQ ID NO: 4) and LLQQLLTE (SEQ ID NO:5).

17. (Withdrawn) An inhibitor according to claim 14 comprising an antibody which specifically binds to a signature motif on a nuclear protein.

18. (Withdrawn) A pharmaceutical composition which comprises an inhibitor as defined in claim 14 or a pharmaceutically-acceptable salt thereof, in association with a pharmaceutically-acceptable diluent or carrier.

19. (Withdrawn) A method of mapping nuclear receptor interaction domains in nuclear proteins in which the method comprises analysis of the sequence of a nuclear protein for the presence of signature motifs as defined in claim 1 in order to identify an interaction domain or a potential interaction domain.

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20. (Withdrawn) A pharmaceutical composition which comprises an inhibitor as defined in claim 15 or a pharmaceutically-acceptable salt thereof, in association with a pharmaceutically-acceptable diluent or carrier.

21. (Withdrawn) A pharmaceutical composition which comprises an inhibitor as defined in claim 16 or a pharmaceutically-acceptable salt thereof, in association with a pharmaceutically-acceptable diluent or carrier.

22. (Withdrawn) A pharmaceutical composition which comprises an inhibitor as defined in claim 17 or a pharmaceutically-acceptable salt thereof, in association with a pharmaceutically-acceptable diluent or carrier.

23. (Cancelled)